

**THE HISTORY OF NEUROPEPTIDE RESEARCH: VERSION 5.a.** A. J. Kastin, J. E. Zadina, R. D. Olson, and W. A. Banks. VA Med. Ctr., Tulane Univ. Sch. Med., and Univ. New Orleans.

Two recent reviews reflect some of the salient points in the history of neuropeptides. One of them focuses on the year of publication of about 25,000 research articles involving peptides and the brain. These were selected from almost 300,000 articles on all aspects of neuroactive peptides published during the last 30 years and emphasize their annual popularity. The other review focuses on more than 400 articles published in a single journal over the last 8 years involving more than 40 central actions of peptides. These are cross-listed, serving to emphasize the multiple actions of peptides. Both of these articles appeared in *Peptides* (15: 367 and 1105, 1994), just one of the 10 journals now published containing the word "peptide" or "peptides" in their titles.

In version 5.a of the history of neuropeptides, the beginning occurs with the demonstration that peripheral injection of a peptide can result in central actions behind the blood-brain barrier (BBB). Unfortunately, except for a "pilot" study with ACTH in hypophysectomized rats by Applezweig and Baudry in 1955, the early studies involving vasopressin and ACTH were confounded by possible secondary effects on blood pressure or release of adrenal steroids. The clearest results involved MSH, which thereby has served as a model for studying the central actions of neuropeptides. Among the many concepts first illustrated with MSH is the ability of peptides to cross the BBB in intact form. Tyr-MIF-1 was the first peptide shown to cross by a selective, saturable transport process.

Other major conceptual boosts to the neuropeptide field came from the discoveries of POMC (the prototypic precursor for peptides including MSH and B-endorphin), of the endogenous opiates and antiopiates themselves, of the neurotrophic effects of some peptides like MSH, of the co-localization of peptides with classical neurotransmitters, and of peptides in amphibian skin with counterparts in the mammalian CNS. The field is still in its infancy.